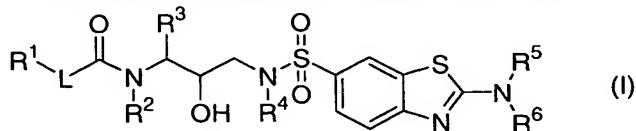


CLAIMS

1. The use of a 2-amino-benzothiazole, having the formula



a *N*-oxide, salt, stereoisomeric form, racemic mixture, prodrug, ester or metabolite

5 thereof, wherein

R₁ is hexahydrofuro[2,3-*b*]furanyl, tetrahydrofuranyl, oxazolyl, thiazolyl, pyridinyl, or phenyl optionally substituted with one or more substituents independently selected from C₁₋₆alkyl, hydroxy, amino, halogen, aminoC₁₋₄alkyl and mono- or di(C₁₋₄alkyl)amino;

10 R₂ is hydrogen or C₁₋₆alkyl;

L is a direct bond, -O-, C₁₋₆alkanediyl-O- or -O-C₁₋₆alkanediyl;

R₃ is phenylC₁₋₄alkyl;

R₄ is C₁₋₆alkyl;

R₅ is hydrogen or C₁₋₆alkyl;

15 R₆ is hydrogen or C₁₋₆alkyl;

in the manufacture of a medicament useful for inhibiting mutant HIV protease in a mammal infected with said mutant HIV protease.

2. The use according to claim 1 wherein

20 R² is hydrogen;

R³ is phenylmethyl;

R⁴ is C₁₋₄alkyl, preferably isobutyl;

R⁵ is hydrogen or methyl;

R⁶ is hydrogen or methyl.

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3. The use according to claim 1 or 2 wherein R⁵ is methyl or hydrogen and R⁶ is hydrogen

4. The use according to any one of claims 1 to 3 wherein both R⁵ and R⁶ are hydrogen.

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5. The use according to any one of claims 1 to 4 wherein -L-R¹ is -O-(hexahydrofuro[2,3-*b*]furanyl), -O-tetrahydrofuranyl, -O-methyl-(optionally substituted phenyl), -O-methyl-pyridinyl, -O-methyl-thiazolyl, -O-methyl-thiazolyl, -methyl-O-(optionally substituted phenyl) or optionally substituted phenyl.

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6. The use according to any one of claims 1 to 5 wherein the compound is {3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester;

5 {3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-carbamic acid thiazol-5-ylmethyl ester;

{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester;

{1-benzyl-3-[(2-dimethylamino-benzothiazole-6-sulfonyl)-isobutyl-amino]-2-hydroxy-propyl}-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester;

10 {3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-carbamic acid benzyl ester;

N-{3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-2-(2,6-dimethyl-phenoxy)-acetamide;

{3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-15 carbamic acid pyridin-3-ylmethyl ester;

3-amino-N-{3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-2-methyl-benzamide;

N-{3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-3-hydroxy-2-methyl-benzamide;

20 {3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-carbamic acid tetrahydro-furan-3-yl ester;

N-{3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-2-methyl-benzamide;

N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-25 propyl}-2-(2,6-dimethyl-phenoxy)-acetamide;

N-{3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-3-fluoro-2-methyl-benzamide;

N-{3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-2-(4-aminomethyl-2,6-dimethyl-phenoxy)-acetamide;

30 {1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-carbamic acid thiazol-5-ylmethyl ester;

3-amino-N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-2-methyl-benzamide;

{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-35 propyl}-carbamic acid tetrahydro-furan-3-yl ester;

N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-3-hydroxy-2-methyl-benzamide;

N-{3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-
2-(4-iodo-2,6-dimethyl-phenoxy)-acetamide;
2-(4-aminomethyl-2,6-dimethyl-phenoxy)-N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-
methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-acetamide;

5 2-(4-amino-2,6-dimethyl-phenoxy)-N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-
methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-acetamide;
N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-
propyl}-4-bromo-2-methyl-benzamide;
{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-
10 propyl}-carbamic acid oxazol-5-ylmethyl ester;
4-amino-N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-
sulfonyl)-amino]-propyl}-3-hydroxy-2-methyl-benzamide;
or a salt, or a stereoisomeric form thereof.

15 7. The use according to any one of claims 1 to 6 wherein the mutant HIV protease has
at least one mutation at a position selected from 10, 71 and 84.

8. The use according to any one of claims 1 to 7 wherein the fold resistance of the
mutant HIV protease for the compound described in any one of claims 1 to 6 ranges
20 between 0.01 and 100.

9. A compound having the formula

a *N*-oxide, salt, stereoisomeric form, racemic mixture, prodrug, ester or metabolite
25 thereof, wherein
R₁ is hexahydrofuro[2,3-*b*]furanyl, tetrahydrofuranyl, oxazolyl, thiazolyl, pyridinyl, or
phenyl optionally substituted with one or more substituents independently
selected from C₁₋₆alkyl, hydroxy, amino, halogen, aminoC₁₋₄alkyl and mono- or
di(C₁₋₄alkyl)amino;

30 R₂ is hydrogen or C₁₋₆alkyl;
L is a direct bond, -O-, C₁₋₆alkanediyl-O- or -O-C₁₋₆alkanediyl;

R₃ is phenylC₁₋₄alkyl;

R₄ is C₁₋₆alkyl;

R₅ is hydrogen or C₁₋₆alkyl;

35 R₆ is hydrogen or C₁₋₆alkyl;

provided that the compound is other than :

{(1S,2R)-3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-carbamic acid benzyl ester;

{(1S,2R)-3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-carbamic acid pyridin-3-ylmethyl ester;

5 {(1S,2R)-3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-carbamic acid thiadiazol-5-ylmethyl ester;

{(1S,2R)-3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-2-(2,6-dimethyl-phenoxy)-acetamide;

10 3-amino-{(1S,2R)-3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-2-methyl-benzamide;

4-amino-{(1S,2R)-3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-2-methyl-benzamide;

5-amino-{(1S,2R)-3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-2-methyl-benzamide;

15 N-{(1S,2R)-3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-2-methyl-benzamide;

N-{(1S,2R)-3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-4-hydroxy-2-methyl-benzamide;

20 N-{(1S,2R)-3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-3-hydroxy-2-methyl-benzamide; and

{(1S,2R)-3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-carbamic acid (S)-(tetrahydrofuran-3-yl) ester.

25 10. A compound according to claim 9 wherein R¹ is hexahydrofuro[2,3-b]furanyl or oxazolyl.

11 A compound according to claim 9 wherein R₁ is hexahydrofuro[2,3-b]furanyl, tetrahydrofuran, oxazolyl, thiazolyl, and L is a direct bond.

30 12. A compound according to claim 9 wherein R₁ is hexahydrofuro[2,3-b]furanyl, oxazolyl, thiazolyl, pyridinyl, or phenyl optionally substituted with one or more substituents independently selected from C₁₋₆alkyl, hydroxy, amino, halogen, aminoC₁₋₄alkyl and mono-or di(C₁₋₄alkyl)amino; and L is -O-.

35 13. A compound according to claim 9 wherein R₁ is hexahydrofuro[2,3-b]furanyl, tetrahydrofuran, oxazolyl, or phenyl substituted with one or more substituents

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independently selected from C₁₋₆alkyl, hydroxy, amino, halogen, aminoC₁₋₄alkyl and mono-or di(C₁₋₄alkyl)amino; and L is C₁₋₆alkanediyl-O- whereby the -O- is attached to the nitrogen of the amide.

5 14. A compound according to claim 9 wherein R₁ is hexahydrofuro[2,3-b]furanyl, tetrahydrofuryl, oxazolyl, thiazolyl, pyridinyl, or phenyl optionally substituted with one or more substituents independently selected from hydroxy, amino, halogen, aminoC₁₋₄alkyl and mono-or di(C₁₋₄alkyl)amino; and L is -O-C₁₋₆alkanediyl whereby -O- is attached to the R¹ group.

10 15. A compound according to any one of claims 9 to 14 wherein at least one of R₅ and R₆ is C₁₋₆alkyl.

15 16. A compound according to any one of claims 9 to 15 wherein R² is hydrogen; R³ is phenylmethyl; R⁴ is C₁₋₄alkyl.

17. a compound according to any one of claims 9 to 16 having the formula {1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester;
20 {1-benzyl-3-[(2-dimethylamino-benzothiazole-6-sulfonyl)-isobutyl-amino]-2-hydroxy-propyl}-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester;
N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-2-(2,6-dimethyl-phenoxy)-acetamide;
N-{3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-
25 3-fluoro-2-methyl-benzamide;
N-{3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-
2-(4-aminomethyl-2,6-dimethyl-phenoxy)-acetamide;
{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-carbamic acid thiazol-5-ylmethyl ester;
30 3-amino-N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-2-methyl-benzamide;
{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-carbamic acid tetrahydro-furan-3-yl ester;
N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-
35 propyl}-3-hydroxy-2-methyl-benzamide;
N-{3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-
2-(4-iodo-2,6-dimethyl-phenoxy)-acetamide;

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2-(4-aminomethyl-2,6-dimethyl-phenoxy)-N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-acetamide;

2-(4-amino-2,6-dimethyl-phenoxy)-N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-acetamide;

5 N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-4-bromo-2-methyl-benzamide;

{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-carbamic acid oxazol-5-ylmethyl ester;

10 4-amino-N-{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-3-hydroxy-2-methyl-benzamide;

a salt thereof, or a stereoisomeric form thereof.

18. A compound according to claim 9 or 10 having the formula
{3-[(2-amino-benzothiazole-6-sulfonyl)-isobutyl-amino]-1-benzyl-2-hydroxypropyl}-

15 carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester;

{1-benzyl-2-hydroxy-3-[isobutyl-(2-methylamino-benzothiazole-6-sulfonyl)-amino]-propyl}-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester;

{1-benzyl-3-[(2-dimethylamino-benzothiazole-6-sulfonyl)-isobutyl-amino]-2-hydroxy-propyl}-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester;

20 or a salt or stereoisomeric form thereof.